

UC Irvine

UC Irvine Previously Published Works

Title

A hypothetical proposal for association between migraine and Meniere's disease.

Permalink

<https://escholarship.org/uc/item/1mf3m0jb>

Authors

Sarna, Brooke
Abouzari, Mehdi
Lin, Harrison W
et al.

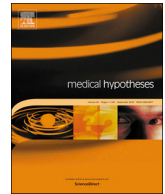
Publication Date

2020

DOI

10.1016/j.mehy.2019.109430

Peer reviewed



A hypothetical proposal for association between migraine and Meniere's disease

Brooke Sarna^{a,1}, Mehdi Abouzari^{a,b,1}, Harrison W. Lin^a, Hamid R. Djalilian^{a,c,*}

^a Department of Otolaryngology–Head and Neck Surgery, University of California, Irvine, USA

^b Division of Pediatric Otolaryngology, Children's Hospital of Orange County, Orange, USA

^c Department of Biomedical Engineering, University of California, Irvine, USA

ARTICLE INFO

Keywords:

Migraine headache
Meniere's disease
Cochleovestibular migraine
Endolymphatic hydrops
Association

ABSTRACT

Meniere's disease (MD) is a chronic condition affecting the inner ear whose precise etiology is currently unknown. We propose the hypothesis that MD is a migraine-related phenomenon which may have implications for future treatment options for both diseases. The association between MD and migraine is both an epidemiological and a mechanistic one, with up to 51% of individuals with MD experiencing migraine compared to 12% in the general population. The presence of endolymphatic hydrops in those with MD may be the factor that unites the two conditions, as hydropic inner ears have an impaired ability to maintain homeostasis. Migraine headaches are theorized to cause aura and symptoms via spreading cortical depression that ultimately results in substance P release, alterations in blood flow, and neurogenic inflammation. Chronically hydropic inner ears are less able to auto-regulate against the changes induced by active migraine attacks and may ultimately manifest as MD. This same vulnerability to derangements in homeostasis may also explain the common triggering factors of both MD attacks and migraine headaches, including stress, weather, and diet. Similarly, it may explain the efficacy of common treatments for both diseases: current migraine treatments such as anti-hypertensives and anti-convulsants have shown promise in managing MD. Though the etiology of both MD and migraine is likely multifactorial, further exploration of the association between the two conditions may illuminate how to best manage them in the future. MD is likely a manifestation of cochleovestibular migraine, which occurs as a result of migraine related changes in both the cochlea and vestibule.

Introduction

Meniere's disease (MD) is a chronic illness first described by Prosper Meniere over 150 years ago that is characterized by a triad of episodic hearing loss, vertigo, and aural symptoms including aural fullness and tinnitus. The condition, which primarily affects the inner ear, causes "attacks" wherein patients experience fluctuating symptomatology lasting as short as 20 min or as long as 24 h. Although diagnostic criteria for the condition classically reference the above triad of symptoms, sufferers may also experience nausea/vomiting, gait disturbance, and headache during these attacks [1]. Eventually, the affected ear may develop progressive and permanent loss of hearing. The prevalence of MD may be as high as 190 people per 100,000, representing over 600,000 sufferers in the United States alone; however, the precise etiology of the disease is not yet known [2].

It was not until 1937, over 70 years after the first descriptions of the disease, that a pathologic correlate of MD was found. By analyzing temporal bone specimens during autopsy, researchers were able to identify endolymphatic hydrops (EH) as a potential marker of MD [3]. Endolymph is a potassium-rich fluid contained within the inner ear that plays a crucial role in both hearing and balance; when there is too much endolymph fluid due to over-production or under-resorption, it is referred to as EH. EH can be broadly divided into categories based on etiology and presence of symptoms: there exist congenital, acquired, and idiopathic forms of EH, and each of these can be symptomatic or asymptomatic [4]. Known causes of EH include congenital malformations, trauma, surgery, infection, and neoplastic processes, but it can also be idiopathic, where there is no known cause or inciting event [5–8]. Recent studies have confirmed the association between idiopathic EH and MD [4,9–12]. Rauch et al. performed a blinded study of

* Corresponding author at: Division of Neurotology and Skull Base Surgery, Department of Otolaryngology–Head and Neck Surgery, University of California Irvine, 19182 Jamboree Road, Otolaryngology-5386, Irvine, CA 92697, USA.

E-mail address: hdjalili@uci.edu (H.R. Djalilian).

¹ These authors contributed equally to this work.

temporal bones and found that all specimens with a clinical diagnosis of MD had idiopathic EH; however, there were 6 specimens with idiopathic EH who had no MD diagnosis [11]. They concluded that their "...results challenge the dogma that endolymphatic hydrops per se generates the symptoms of Meniere's syndrome" [11]. It appears that although sufferers of MD will in all cases have at least one ear with hydrops, not every individual with EH experiences the symptoms of MD. This finding has led to the conclusion that there must be another factor at play that induces those with EH to develop MD.

Multiple hypotheses have been proposed to explain this outlying factor. Membrane rupture causing contamination of perilymph with potassium-rich endolymph, mechanical damage by EH, and vascular phenomena have all at times been theorized to cause MD [3,4,13]. Recent evidence has refuted the hypothesis that potassium intoxication of perilymph might explain MD, as well as the theory that EH alone is responsible for MD [10,14,15]. This has led to recent popularization of the theory that MD may be related to vascular or ischemic conditions that affect perfusion of the inner ear during attacks. One such condition is migraine headaches, which appear to have a partly vascular component to their manifestation and have been found in close association with MD [16–19]. In this paper, we propose that MD is indeed related to the phenomenon that is migraine, and that treatments traditionally used for migraine headache can be applied to effectively treat MD as well.

Hypothesis

Our hypothesis posits that MD is in fact a migraine-related phenomenon, with both conditions united by a common unknown, though potentially vasculogenic or related to spreading cortical depression, pathophysiology or risk factor that can predispose to development of both diseases. This common risk factor can cause those with otherwise asymptomatic EH to develop MD and potentially progressive hearing loss. This theory helps explain the significant association of MD with migraine and the similarity of triggering factors in both diseases. Furthermore, it can help explain the efficacy of current treatments for MD as well as provide a steppingstone for future management and treatment options.

Evaluation of the hypothesis

An epidemiological and mechanistic association between Meniere's disease and migraine

Though not every individual with MD will experience migraine and not every individual with migraine will develop MD, there is a significant association of MD with migraine headaches. The association of migraine with MD dates to MD's origins in 1861, when Prosper Meniere first described the condition. In addition to the triad of symptoms used to characterize MD, Meniere also described migraine headaches and migraine auras occurring in the very same patient population he used to elucidate the symptoms of MD [20]. Though the prevalence of migraine symptoms in this historical population is not known, recent studies have further explored this connection and determined that up to 51% of MD sufferers also suffer from migraine headaches [21] and that up to 45% of MD patients experience migraine symptoms during an attack [17]. Familial clustering of migraine and MD has also been found, supporting a relationship between the two diagnoses [22].

In addition, migraine is associated with inner ear pathologies, including vertigo, tinnitus, and even sudden sensorineural hearing loss [23]. Two disease entities – vestibular migraine and cochlear migraine – have been proposed that illustrate the interplay between migraine and inner ear symptoms. Vestibular migraine encompasses migraine and vertigo symptoms, and cochlear migraine encompasses migraine and auditory symptoms [24,25]. When experienced together, they form a symptom complex we term cochleovestibular migraine that is similar in

presentation to MD [25].

The connection is not merely an epidemiological one but a mechanistic one as well. As part of a migraine attack, spreading cortical depression causes release of neuropeptides and cytokines including calcitonin gene-related peptide and substance P from the trigeminal ganglion, leading to vasodilation, increased vascular permeability, and extravasation of plasma [26–28]. This contributes to the neurogenic inflammation and pain that occurs during the headache phase of a migraine. Innervation of the cochlea and cochlear blood vessels by trigeminal nerve fibers has been previously demonstrated, supporting the notion that vascular effects of migraine can extend to affect the inner ear as well [29–31]. To add another layer of complexity, the response of inner ears with EH to substance P differs from that of non-hydrotic inner ears. Specifically, chronically hydrotic inner ears appear to lose their ability to autoregulate their vasculature and blood flow, making them more vulnerable to other stress factors such as those detailed below [32–35]. This could potentially cause those with existing neuropeptide and vasomotor dysfunction in the trigeminal nerve, such as in migraine, to manifest MD. In fact, individuals with concurrent migraine and MD appear to have a younger age of onset of MD and are more likely to experience bilateral hearing loss and aural fullness [36].

Specific case studies have also demonstrated a link between migraine and inner ear pathologies. In one case, migraine-associated vascular changes may have caused inner ear ischemia and EH, ultimately resulting in sensorineural hearing loss and MD-like symptoms [37]. In another, an individual with migraine-associated hearing loss was found to have severe bilateral EH [38]. Both migraine and MD have also been found in association with drop attacks, though the prevalence of drop attacks is rare in both conditions and sometimes is associated with neither [39,40]. Vascular factors that play a role in migraine may indeed predispose to earlier development of MD and manifestation of more inner ear symptoms.

Meniere's disease and migraine share similar triggers

In addition to the epidemiologic and mechanistic association of MD and migraine, both conditions also share common triggering factors, including stress, weather changes, and dietary intake. Multiple studies have found an association between stress levels and migraine occurrence, which may be related to the observed ability of steroids to increase the frequency of spreading cortical depression events in the presence of certain genetic mutations [41–43]. This can be extrapolated to provide an explanation for why physiologic stressors such as acute illness, poor sleep quality, and new onset pain disorders, among other things, can provoke or worsen migraine and MD. Fluctuations in estrogen may also contribute to spreading cortical depression and thus both migraine and MD symptoms. Vestibular migraine in particular has a similar age of onset as MD in the fifth decade of life, and both migraine and vestibular migraine occur more frequently in women [44,45]. Sudden decreases in estrogen level, such as those that can occur *peri-menopause*, can provoke migraine, and certain female mice in the presence of estrogen have been observed to have faster and more frequent cortical spreading depression events [46,47]. Weather effects including low atmospheric pressure, high temperatures, low humidity, and increased light intensity during summer months have also been linked to increased migraine frequency [48–51]. Finally, caffeine has been reported to trigger migraine as well. Similarly, stress and low atmospheric pressure have been linked to MD attacks [52–54], and caffeine consumption was associated with a lower age of onset of MD [55]. To further unite the two diagnoses, strong odors and visual motion such as driving or watching television have been identified as triggers for both migraine and MD [21,56]. While alcohol and sodium restriction have traditionally been recommended in the management of MD and have shown some efficacy [57], there have yet to be studies critically evaluating the effect of these specific dietary changes on MD.

Some studies have failed to show a link between dietary sodium intake and migraine occurrence, and rather the effect may be from lack of sufficient water intake or from nitrites, glutamate, or tyramine that may be found in high-sodium-content foods [42,58,59].

In fact, both tyramine and caffeine are known vasoconstrictors and hypertensive agents that may be one of the factors to which hydropic inner ears are more susceptible [60]. Caffeine promotes vasoconstriction and decreased blood flow that normally is compensated for by adenosine receptors [61]. With Long term use, however, the impaired autoregulation of blood flow in hydropic ears may prevent adaptation and allow for easier provocation of both migraine and MD. This may also explain why fermented, tyramine-containing alcohol could worsen both conditions, and how abstaining from fermented alcohol and caffeine may improve symptomatology.

Treatments traditionally reserved for migraine may help treat Meniere's disease

Current migraine treatment options, including both medical and surgical treatments, have shown success in treating MD and inner ear symptomatology. Anti-hypertensive drugs including calcium channel blockers and beta blockers are options for prophylactic treatment of migraine [62,63]. Other anti-hypertensive diuretics such as carbonic anhydrase inhibitors and hydrochlorothiazide can be used as treatment options for MD, though evidence for efficacy varies [57,64,65]. This may represent the commonality of vascular factors in both migraine and MD. Furthermore, by controlling diet for compounds that promote migraine, particularly caffeine, glutamate, and tyramine, and for dehydration, migraine and MD symptoms can be reduced [66]. Tricyclic antidepressants (e.g., nortriptyline) and anti-convulsants such as topiramate have been successfully used to manage MD symptoms as well, most likely through a variety of mechanisms including neuromodulation and inhibition of certain subtypes of carbonic anhydrase enzymes [67,68]. Oral and parenteral steroids, which may help prevent spreading cortical depression and the release of inflammatory mediators that can affect the inner ear, have also been used to manage both acute migraine and MD [19,69,70].

Surgical treatment options such as tympanostomy tubes may alleviate both MD attacks and inner ear manifestations of migraine by preventing changes in barometric pressure from triggering acute events. This treatment has already shown some ability to alleviate vertigo symptoms in MD and remains effective for approximately 47% of patients [71–73]. Interestingly, the percentage of migraine sufferers who report weather as a trigger also falls within the 40–60% range [48,74,75]. Though the mechanism is not completely understood, changes in barometric pressure have been demonstrated to provoke neuropathic pain in rats [76]. If the inner ear is lesioned, changes in pressure no longer worsen neuropathic pain [77]. This suggests that the inner ear is profoundly affected by changes in atmospheric pressure, which are sensed at the tympanic membrane, and may instigate migraine and MD attacks, particularly in those with EH who are already more susceptible to perturbations in homeostasis. Removal of the tympanic membrane's ability to sense pressure by placing a tympanostomy tube can allow for elimination of barometric pressure changes as a trigger for both conditions.

Migraine's association with inner ear symptoms may also explain why treatments traditionally used for migraine have shown effectiveness when applied to inner ear pathologies: migraine prophylactic medications have been successfully used to treat aural fullness, post-stapedectomy-vertigo, and mal de débarquement syndrome [78–80].

Discussion and conclusion

The association between MD and migraine headache suggests an underlying factor that unites them both; however, the precise etiology is not yet fully known. Evidence continues to emerge exploring various

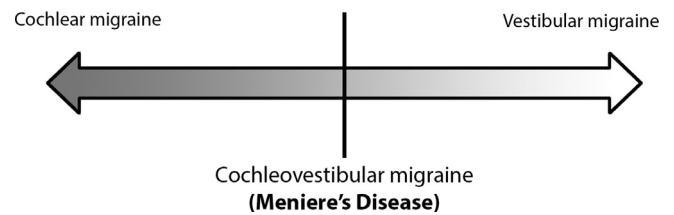


Fig. 1. Spectrum of migraine inner ear disease. Meniere's disease most resembles a combination of symptoms from both cochlear and vestibular migraine and may exist on a continuum with the two conditions.

contributing factors of both MD and migraine, including spreading cortical depression, vasculopathies, neuropeptide derangements, hormonal interactions, calcium channelopathies, and salt metabolism [19,81,82]. Though the true cause may be multifactorial, it is likely that the underlying triggers cause both MD and migraine depending on the individual, and in the case of MD, those with existing EH may be more susceptible. Rather than existing as separate conditions, MD and migraine inner ear disorder may instead exist on a continuum (Fig. 1). At one end are patients with purely vestibular symptoms (e.g., vertigo, motion sensitivity, imbalance), termed vestibular migraine. At the other end of the spectrum are patients who have purely cochlear symptoms (e.g., fluctuating hearing loss, aural pressure, tinnitus, hyperacusis). The patients who have the combination of both symptoms are patients with cochleovestibular migraine, or Meniere's disease.

As of yet, there is no definitive cure for MD, but treatments traditionally used for migraine have shown promise in improving quality of life [67]. Through further exploration of the association between migraine and MD, it may be possible to find more effective treatments and management techniques. Subsequent studies evaluating the treatment efficacy of dietary changes, the precise link between migraine, cortical depression, and inner ear pathologies, and, eventually, the pathophysiology of migraine itself may better illuminate the relationship between MD and migraine, potentially revealing how to best manage and cure MD in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Mehdi Abouzari, MD, PhD; is supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant TL1TR001415-04. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2019.109427>.

References

- [1] Lopez-Escamez JA, Carey J, Chung WH, Goebel JA, Magnusson M, Mandala M, et al. Diagnostic criteria for Meniere's disease. *J Vestib Res* 2015;25(1):1–7.
- [2] Havia M, Kentala E, Pyrkko I. Prevalence of meniere's disease in general population of Southern Finland. *Otolaryngol Head Neck Surg* 2005;133(5):762–8.
- [3] Hallpike CS, Cairns H. Observations on the pathology of meniere's syndrome: (Section of Otolaryngology). *Proc R Soc Med* 1938;31(11):1317–36.
- [4] Schuknecht HF, Gulya AJ. Endolymphatic hydrops. An overview and classification. *Ann Otol Rhinol Laryngol Suppl* 1983;106:1–20.
- [5] Calenoff E, Zhao JC, Derlacki EL, Harrison WH, Selmeczi K, Dutra JC, et al. Patients with Meniere's disease possess IgE reacting with herpes family viruses. *Arch*

- Otolaryngol Head Neck Surg 1995;121(8):861–4.
- [6] DiBiase P, Arriaga MA. Post-traumatic hydrops. *Otolaryngol Clin North Am* 1997;30(6):1117–22.
 - [7] Klockars T, Kentala E. Inheritance of Meniere's disease in the Finnish population. *Arch Otolaryngol Head Neck Surg* 2007;133(1):74–7.
 - [8] Yamamoto E, Mizukami C. Development of the vestibular aqueduct in Meniere's disease. *Acta Otolaryngol Suppl* 1993;504:46–50.
 - [9] Foster CA, Breeze RE. Endolymphatic hydrops in Meniere's disease: cause, consequence, or epiphenomenon? *Otol Neurotol* 2013;34(7):1210–4.
 - [10] Merchant SN, Adams JC, Nadol Jr. JB. Pathophysiology of Meniere's syndrome: are symptoms caused by endolymphatic hydrops? *Otol Neurotol* 2005;26(1):74–81.
 - [11] Rauch SD, Merchant SN, Thedinger BA. Meniere's syndrome and endolymphatic hydrops. Double-blind temporal bone study. *Ann Otol Rhinol Laryngol* 1989;98(11):873–83.
 - [12] Gurkov R, Pytko I, Zou J, Kentala E. What is Meniere's disease? A contemporary re-evaluation of endolymphatic hydrops. *J Neurol* 2016;263(Suppl 1):S71–81.
 - [13] Lempert J, Wolff D, Rambo JH, Wever EG, Lawrence M. New theory for the correlation of the pathology and the symptomatology of Meniere's disease; a research study of the vestibular endolymphatic labyrinth. *Ann Otol Rhinol Laryngol* 1952;61(3):717–46.
 - [14] Brown DH, McClure JA, Downar-Zapolski Z. The membrane rupture theory of Meniere's disease—is it valid? *Laryngoscope* 1988;98(6 Pt 1):599–601.
 - [15] Mancini F, Catalani M, Carru M, Monti B. History of Meniere's disease and its clinical presentation. *Otolaryngol Clin North Am* 2002;35(3):565–80.
 - [16] Charles A, Brennan KC. The neurobiology of migraine. *Handb Clin Neurol* 2010;97:99–108.
 - [17] Radtke A, Lempert T, Gresty MA, Brookes GB, Bronstein AM, Neuhauser H. Migraine and Meniere's disease: is there a link? *Neurology* 2002;59(11):1700–4.
 - [18] Rassekh CH, Harker LA. The prevalence of migraine in Meniere's disease. *Laryngoscope* 1992;102(2):135–8.
 - [19] Charles A. The pathophysiology of migraine: implications for clinical management. *Lancet Neurol* 2018;17(2):174–82.
 - [20] Moshtaghi O, Sahyouni R, Lin HW, Ghavami Y, Djalilian HR. A historical recount: discovering meniere's disease and its association with migraine headaches. *Otol Neurotol* 2016;37(8):1199–203.
 - [21] Ghavami Y, Mahboubi H, Yau AY, Maducdoc M, Djalilian HR. Migraine features in patients with Meniere's disease. *Laryngoscope* 2016;126(1):163–8.
 - [22] Cha YH, Kane MJ, Baloh RW. Familial clustering of migraine, episodic vertigo, and Meniere's disease. *Otol Neurotol* 2008;29(1):93–6.
 - [23] Chu CH, Liu CJ, Fuh JL, Shiao AS, Chen TJ, Wang SJ. Migraine is a risk factor for sudden sensorineural hearing loss: a nationwide population-based study. *Cephalalgia* 2013;33(2):80–6.
 - [24] Dieterich M, Obermann M, Celebisoy N. Vestibular migraine: the most frequent entity of episodic vertigo. *J Neurol* 2016;263(Suppl 1):S82–9.
 - [25] Hwang JH, Tsai SJ, Liu TC, Chen YC, Lai JT. Association of tinnitus and other cochlear disorders with a history of migraines. *JAMA Otolaryngol Head Neck Surg* 2018;144(8):712–7.
 - [26] Malhotra R. Understanding migraine: potential role of neurogenic inflammation. *Ann Indian Acad Neurol* 2016;19(2):175–82.
 - [27] Harriott AM, Takizawa T, Chung DY, Chen SP. Spreading depression as a preclinical model of migraine. *J Headache Pain* 2019;20(1):45.
 - [28] Brain SD, Grant AD. Vascular actions of calcitonin gene-related peptide and adenosine. *Physiol Rev* 2004;84(3):903–34.
 - [29] Vass Z, Shore SE, Nuttall AL, Jancso G, Brechtelsbauer PB, Miller JM. Trigeminal ganglion innervation of the cochlea—a retrograde transport study. *Neuroscience* 1997;79(2):605–15.
 - [30] Vass Z, Shore SE, Nuttall AL, Miller JM. Direct evidence of trigeminal innervation of the cochlear blood vessels. *Neuroscience* 1998;84(2):559–67.
 - [31] Vass Z, Steyger PS, Hordichok AJ, Trune DR, Jancso G, Nuttall AL. Capsaicin stimulation of the cochlea and electric stimulation of the trigeminal ganglion mediate vascular permeability in cochlear and vertebro-basilar arteries: a potential cause of inner ear dysfunction in headache. *Neuroscience* 2001;103(1):189–201.
 - [32] Brechtelsbauer PB, Ren TY, Miller JM, Nuttall AL. Autoregulation of cochlear blood flow in the hydropic guinea pig. *Hear Res* 1995;89(1–2):130–6.
 - [33] Miller JM, Ren TY, Nuttall AL. Studies of inner ear blood flow in animals and human beings. *Otolaryngol Head Neck Surg* 1995;112(1):101–13.
 - [34] Ren T, Laurikainen E, Quirk WS, Miller JM, Nuttall AL. Effects of stellate ganglion stimulation on bilateral cochlear blood flow. *Ann Otol Rhinol Laryngol* 1993;102(5):378–84.
 - [35] Vass Z, Dai CF, Steyger PS, Jancso G, Trune DR, Nuttall AL. Co-localization of the vanilloid capsaicin receptor and substance P in sensory nerve fibers innervating cochlear and vertebro-basilar arteries. *Neuroscience* 2004;124(4):919–27.
 - [36] Cha YH, Brodsky J, Ishiyama G, Sabatti C, Baloh RW. The relevance of migraine in patients with Meniere's disease. *Acta Otolaryngol* 2007;127(12):1241–5.
 - [37] Lee H, Lopez I, Ishiyama A, Baloh RW. Can migraine damage the inner ear? *Arch Neurol* 2000;57(11):1631–4.
 - [38] Liu IY, Ishiyama A, Sepahdari AR, Johnson K, Ishiyama G. Bilateral endolymphatic hydrops in a patient with migraine variant without vertigo: a case report. *Headache* 2017;57(3):455–9.
 - [39] Ishiyama G, Ishiyama A, Baloh RW. Drop attacks and vertigo secondary to a non-menièrè otologic cause. *Arch Neurol* 2003;60(1):71–5.
 - [40] Brantberg K, Baloh RW. Similarity of vertigo attacks due to Meniere's disease and benign recurrent vertigo, both with and without migraine. *Acta Otolaryngol* 2011;131(7):722–7.
 - [41] Meng ID, Cao L. From migraine to chronic daily headache: the biological basis of headache transformation. *Headache* 2007;47(8):1251–8.
 - [42] Wober C, Holzhammer J, Zeitlhofer J, Wessely P, Wober-Bingol C. Trigger factors of migraine and tension-type headache: experience and knowledge of the patients. *J Headache Pain* 2006;7(4):188–95.
 - [43] Shyti R, Eikermann-Haerter K, van Heiningen SH, Meijer OC, Ayata C, Joels M, et al. Stress hormone corticosterone enhances susceptibility to cortical spreading depression in familial hemiplegic migraine type 1 mutant mice. *Exp Neurol* 2015;263:214–20.
 - [44] Formeister EJ, Rizk HG, Kohn MA, Sharon JD. The epidemiology of vestibular migraine: a population-based survey study. *Otol Neurotol* 2018;39(8):1037–44.
 - [45] da Costa SS, de Sousa LC, Piza MR. Meniere's disease: overview, epidemiology, and natural history. *Otolaryngol Clin North Am* 2002;35(3):455–95.
 - [46] Allais G, Chiarle G, Sinigaglia S, Airola G, Schiapparelli P, Benedetto C. Estrogen, migraine, and vascular risk. *Neurol Sci* 2018;39(Suppl 1):11–20.
 - [47] Pietrobon D, Brennan KC. Genetic mouse models of migraine. *J Headache Pain* 2019;20(1):79.
 - [48] Hoffmann J, Lo H, Neeb L, Martus P, Reuter U. Weather sensitivity in migraineurs. *J Neurol* 2011;258(4):596–602.
 - [49] Marmura MJ, Hernandez PB. High-altitude headache. *Curr Pain Headache Rep* 2015;19(5):483.
 - [50] Salvesen R, Bekkelund SI. Migraine, as compared to other headaches, is worse during midnight-sun summer than during polar night. A questionnaire study in an Arctic population. *Headache* 2000;40(10):824–9.
 - [51] Yilmaz M, Gurger M, Atescelik M, Yildiz M, Gurbuz S. Meteorologic parameters and migraine headache: ED study. *Am J Emerg Med* 2015;33(3):409–13.
 - [52] Andersson G, Haggebo C, Yardley L. Stress and symptoms of Meniere's disease: a time-series analysis. *J Psychosom Res* 1997;43(6):595–603.
 - [53] Schmidt W, Sarraf C, Ronan N, Barrett G, Whinney DJ, Fleming LE, et al. The weather and meniere's disease: a longitudinal analysis in the UK. *Otol Neurotol* 2017;38(2):225–33.
 - [54] Soderman AC, Moller J, Bagger-Sjoberg D, Bergenius J, Hallqvist J. Stress as a trigger of attacks in Meniere's disease. A case-crossover study. *Laryngoscope* 2004;114(10):1843–8.
 - [55] Sanchez-Sellero I, San-Roman-Rodriguez E, Santos-Perez S, Rossi-Izquierdo M, Soto-Varela A. Caffeine intake and Meniere's disease: is there relationship? *Nutr Neurosci* 2018;21(9):624–31.
 - [56] Silva-Neto RP, Peres MF, Valença MM. Odorant substances that trigger headaches in migraine patients. *Cephalalgia* 2014;34(1):14–21.
 - [57] Sheih F, Christov F, Gluth MB. Newly diagnosed meniere's Disease: clinical course with initiation of noninvasive treatment including an accounting of vestibular migraine. *Ann Otol Rhinol Laryngol* 2018;127(5):331–7.
 - [58] Pogoda JM, Gross NB, Arakaki X, Fonteh AN, Cowan RP, Harrington MG. Severe headache or migraine history is inversely correlated with dietary sodium intake: NHANES 1999–2004. *Headache* 2016;56(4):688–98.
 - [59] Kohlenberg RJ. Tyramine sensitivity in dietary migraine: a critical review. *Headache* 1982;22(1):30–4.
 - [60] Pelligrino DA, Xu HL, Vetri F. Caffeine and the control of cerebral hemodynamics. *J Alzheimers Dis* 2010;20(Suppl 1):S51–62.
 - [61] Addicott MA, Yang LL, Peiffer AM, Burnett LR, Burdette JH, Chen MY, et al. The effect of daily caffeine use on cerebral blood flow: how much caffeine can we tolerate? *Hum Brain Mapp* 2009;30(10):3102–14.
 - [62] Loder E, Rizzoli P. Pharmacologic prevention of migraine: a narrative review of the state of the art in 2018. *Headache* 2018;58(Suppl 3):218–29.
 - [63] Shamlan TA, Choi JY, Ramakrishnan R, Miller JB, Wang SY, Taylor FR, et al. Preventive pharmacologic treatments for episodic migraine in adults. *J Gen Intern Med* 2013;28(9):1225–37.
 - [64] Syed I, Aldren C. Meniere's disease: an evidence based approach to assessment and management. *Int J Clin Pract* 2012;66(2):166–70.
 - [65] Akiyama H, Hasegawa Y. Migraine treated using a prophylactic combination of candesartan and hydrochlorothiazide (ECARD Combination Tablets LD). *Pain Pract* 2013;13(7):566–71.
 - [66] Abouzari M, Abiri A, Djalilian HR. Successful treatment of a child with definite Meniere's disease with the migraine regimen. *Am J Otolaryngol* 2019.
 - [67] Ghavami Y, Haidar YM, Moshtaghi O, Lin HW, Djalilian HR. Evaluating quality of life in patients with meniere's disease treated as migraine. *Ann Otol Rhinol Laryngol* 2018;127(12):877–87.
 - [68] Shank RP, Gardocki JF, Streeter AJ, Maryanoff BE. An overview of the preclinical aspects of topiramate: pharmacology, pharmacokinetics, and mechanism of action. *Epilepsia* 2000;41(Suppl 1):S3–9.
 - [69] Seidman MD, Vivek P. Intratympanic treatment of hearing loss with novel and traditional agents. *Otolaryngol Clin North Am* 2004;37(5):973–90.
 - [70] Woldeamanuel YW, Rapoport AM, Cowan RP. The place of corticosteroids in migraine attack management: a 65-year systematic review with pooled analysis and critical appraisal. *Cephalalgia* 2015;35(11):996–1024.
 - [71] Montandon P, Guillemin P, Hausler R. Prevention of vertigo in Meniere's syndrome by means of transtympanic ventilation tubes. *ORL J Otorhinolaryngol Relat Spec* 1988;50(6):377–81.
 - [72] Sugawara K, Kitamura K, Ishida T, Sejima T. Insertion of tympanic ventilation tubes as a treating modality for patients with Meniere's disease: a short- and long-term follow-up study in seven cases. *Auris Nasus Larynx* 2003;30(1):25–8.
 - [73] Ogawa Y, Otsuka K, Hagiwara A, Inagaki A, Shimizu S, Nagai N, et al. Clinical study of tympanostomy tube placement for patients with intractable Meniere's disease. *J Laryngol Otol* 2015;129(2):120–5.
 - [74] Turner LC, Molgaard CA, Gardner CH, Rothrock JF, Stang PE. Migraine trigger factors in non-clinical Mexican-American population in San Diego county: implications for etiology. *Cephalalgia* 1995;15(6):523–30.
 - [75] Kelman L. The triggers or precipitants of the acute migraine attack. *Cephalalgia*

- 2007;27(5):394–402.
- [76] Funakubo M, Sato J, Obata K, Mizumura K. The rate and magnitude of atmospheric pressure change that aggravate pain-related behavior of nerve injured rats. *Int J Biometeorol* 2011;55(3):319–26.
- [77] Funakubo M, Sato J, Honda T, Mizumura K. The inner ear is involved in the aggravation of nociceptive behavior induced by lowering barometric pressure of nerve injured rats. *Eur J Pain* 2010;14(1):32–9.
- [78] Ghavami Y, Haidar YM, Ziai KN, Moshtaghi O, Bhatt J, Lin HW, et al. Management of mal de débarquement syndrome as vestibular migraines. *Laryngoscope* 2017;127(7):1670–5.
- [79] Moshtaghi O, Ghavami Y, Mahboubi H, Sahyouni R, Haidar Y, Ziai K, et al. Migraine-related aural fullness: a potential clinical entity. *Otolaryngol Head Neck Surg* 2018;158(1):100–2.
- [80] Moshtaghi O, Mahboubi H, Haidar YM, Sahyouni R, Lin HW, Djalilian HR. Resolution of persistent post-stapedotomy vertigo with migraine prophylactic medication. *Otol Neurotol* 2017;38(10):1500–4.
- [81] Baloh RW. Neurotology of migraine. *Headache* 1997;37(10):615–21.
- [82] Campbell DA, Hay KM, Tonks EM. An investigation of the salt and water balance in migraine. *Br Med J* 1951;2(4745):1424–9.